this is due to pain causing loss of muscle strength in knee OA, rather than loss of muscle strength causing structural progression of knee OA to higher KL grades.

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IMPAIRED MUSCLE FUNCTION IN A MOUSE SURGICAL MODEL OF OSTEOARTHRITIS

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Purpose: Osteoarthritis (OA) is typically characterised by progressive loss of articular cartilage and aberrant bone formation. However, in knee OA in particular, loss of muscle mass, strength and function is also common and this contributes to impaired quality of life through deterioration of functional capacity. Our previous studies in knee OA patients have shown that reduced muscle strength and altered walking pattern is associated with increased expression of pro-inflammatory cytokines and signalling molecules. It is not clear if the loss of muscle mass and strength in knee OA occurs as a result of reduced limb use, or if the muscle itself is a direct target of the OA degenerative processes. In order to better understand the relationship between OA and muscle function, we examined the changes in muscle function during the onset and progression of OA in a mouse surgical model of OA (destabilisation of the medial meniscus, DMM-OA)

Methods: Male C57BL/6 mice underwent DMM or sham surgery on the right knee only. Tibialis anterior (TA) muscle function was assessed in situ at 1, 4 and 8 weeks post surgery ($n = 6$ sham and 6 DMM-OA mice per timepoint). Parameters measured : tetanic forces - absolute force (Po) and specific force (sPo, normalized to muscle mass); twitch force measurements - twitch force production (Pt), time to peak (TPT) and time taken to relax to 50% of peak twitch force (1/2RT). Importantly, the TA muscle is not impacted directly by the surgical procedure. Joint damage and synovial inflammation were assessed by histology. Statistics: Multivariate analysis of variance (MANOVA) with Bonferroni correction was used to examine the differences within groups for the 3 time points.

Results: DMM surgery results in destabilization of the knee joint leading to increased loading within the medial compartment of the knee joint. By 4 weeks post-surgery, proteoglycan loss, subchondral bone accrual and osteophyte formation are evident with significant cartilage erosion present at 8 weeks post surgery. Inflammation of the synovial lining due to surgery subsides in both the sham and DMM-OA knee joints by 4 weeks post surgery, but a thickened synovial lining layer remains within DMM-OA joints. At 1 week post surgery, there was no difference in either the tetanic or twitch force parameters between the DMM-OA and SHAM TA muscle. However both DMM-OA and SHAM TA muscles showed improvement in their tetanic and twitch force parameters with time suggesting an effect of the surgery itself on muscle function. The tetanic parameters absolute force (Po) and specific force (sPo), were reduced in DMM-OA muscle compared to sham muscle at both 4 weeks and 8 weeks post surgery ($P<0.05$). At 4 and 8 weeks post surgery there was no significant difference between DMM-OA and sham muscles in the twitch response, time to peak tension (TPT). At 8 weeks post surgery the twitch force (Pt) was reduced in DMM-OA muscle compared to sham. Furthermore, the time taken to relax to 50% of peak twitch force (1/2RT) was increased in DMM-OA muscle compared to sham muscle at 8 weeks ($P<0.001$).

Conclusions: Our studies demonstrate that function of the TA muscle is impaired in DMM OA when compared to sham controls. Although tetanic force responses were reduced early during OA progression (starting at 4 weeks post-surgery) the greatest changes, including the twitch force responses, were evident at the later stage of OA (8 weeks post surgery) when cartilage erosion is evident. This suggests that similar to human OA, muscle function in the DMM model of OA deteriorates with worsening OA joint damage. We are yet to determine the direct cause of this alteration in muscle function, and its relationship with pain and gait. However, further investigation of these changes in the DMM model of OA, may yield insight into the mechanisms mediating muscle degeneration in human knee OA, potentially leading to the identification of improved rehabilitation strategies for these patients.

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PROSPECTIVE SPATIAL PATTERNS OF TIBIAL CARTILAGE THICKNESS CHANGES FOLLOWING ACL RECONSTRUCTION

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Purpose: Rupture of the anterior cruciate ligament (ACL) often leads to premature osteoarthritis (OA) even following surgical reconstruction. Identifying the conditions that lead to early cartilage breakdown has been challenging as clinical symptoms of OA are often not detectable for 10 years or more after the index injury. Yet it would be useful to quantify early changes in cartilage morphology at an early stage following ACL injury to help identify early risk factors for subsequent progression to OA. Early cartilage changes can include regional cartilage thickening and thinning. As such the spatial patterns of cartilage thickness would be sensitive morphological markers of change. Thus the spatial pattern of the cartilage thickness map can provide important information not available with other methods.

The objective of this study was test the hypothesis that the pattern of thickness change would reflect a consistent pattern of change between two and four years following ACL reconstruction with progressively larger differences at four.

Methods: 23 unilateral ACLR subjects (11 F, 28 yrs, 1.7 m, 72 kg, tested at 2.5 and 4.6 yrs from injury) and 23 matched controls participated in this study after providing IRB-approved informed consent. Three-dimensional tibial cartilage models were obtained for both knees of all participants from MR images (1.5T, 3D SPGR). A shape matching technique was applied to convert the models into two-dimensional anatomically-standardized thickness maps. Side-to-side difference thickness maps were computed to present the mean difference between ACLR and contralateral knees, both at two and four years from reconstruction. A side-to-side difference map was also calculated for the healthy controls by randomly dividing left and right knees into two groups. Statistical parametric mapping (SPM) was used to identify regions of significant differences between two groups of 23 paired thickness maps (smoothness-adjusted $\alpha = 0.05$).

Results: There was a significantly thinner region in the lateral compartment (avg. -0.4 mm) and a significantly thicker region in the medial compartment (avg. 0.2 mm) for ACLR compared to contralateral knees at four years from surgery. There were no significant differences in thickness between both knees of the healthy controls or between ACLR and contralateral knees at two years from reconstruction (Fig. 1). However, the spatial variations in side-to-side differences were consistent between two and four years following reconstruction.

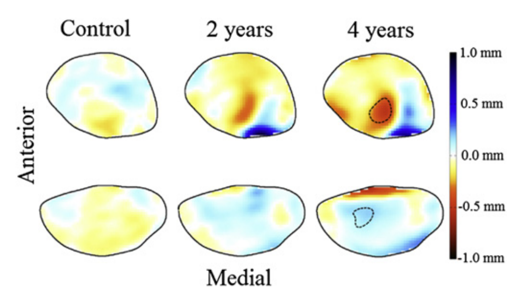

Figure 1. Left: side-to-side cartilage thickness difference map (random selection between left and right knees) for the healthy controls. Center & Right: side-to-side cartilage thickness difference maps (ACLR minus contralateral knees) at two and four years from reconstruction. Areas outlined with dotted line in the four years map represent regions of significant difference (adjusted $p< 0.05$).

Conclusion: Detectable differences in tibial cartilage thickness could be identified at four years following reconstruction using this spatial patterning method. It is important to note that the spatial variations in thickness differences were similar at two years to those present at four years from injury, suggesting a pattern of thickness change following ACL reconstruction can be characterized. The spatial thickness distribution method of this study allows for detailed display of differences which may not be detected with conventionally defined regions of mean thickness.